

Amyloidosis in cheetahs (*Acinonyx jubatus*), transmissible?

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ABSTRACT

Amyloidosis causes pathology through the accumulation of misfolded amyloid A protein in visceral organs, often leading to death of the animal. The increase of amyloidosis in captive cheetahs is of grave concern for the species, yet nothing is definitively known about its mechanism of transmission. One hypothesis is that amyloidosis is transmissible. Cheetah demographic and disease data were analyzed to determine the likelihood that amyloidosis is infectious. While our analysis does not disprove the infectious transmission route, simple transmission is not supported based on our findings.



INTRODUCTION

Acinonyx jubatus

The wild cheetah (*Acinonyx jubatus*) population is thought to have declined over 30% in the last 18 years, with an estimated 10,000 total cheetahs remaining.¹ Poor genetic diversity has been proposed to be the cause of increased disease susceptibility, increased juvenile mortality, and low reproductive fitness in captivity.^{2,3,4} Thus, preservation of the species is important, and any diseases affecting cheetahs could be devastating to the remaining populations.

Amyloidosis

Systemic AA amyloidosis is considered to be a major cause of morbidity and mortality among captive cheetah populations with an estimated prevalence of 70% in 1995, increased from 20% pre-1990.^{2,3,5} Amyloidoses are chronic, protein misfolding diseases, caused by the deposition and aggregation of the protein in visceral organs such as the liver and kidney, resulting in organ failure and death.^{2,6,7} Despite the high prevalence and fatal consequences of amyloidosis in cheetahs, little is known about the etiology and transmission of AA amyloidosis.

Hypothesis

One hypothesis for the disease etiology is that amyloidosis transmits amongst cheetahs, similar to the way chronic wasting disease is thought to transmit in cervids. Zhang et al. (2008) found AA amyloid fibrils in cheetah feces that were infective in rodents, which supports this hypothesis. The focus of our research was to test the hypothesis of transmissibility through analysis of data from the captive cheetah population in the United States.

METHODS

Six zoos were included in this study: Cincinnati, Columbus, Fossil Rim, White Oak, Wildlife Safari, and The Wilds .

Odds Ratio Calculations

The risk of transmission among cheetahs co-habiting in a zoo for different lengths of time was quantified using odds ratios. Levels of exposure to known infected cheetahs were: high (>30 cheetah days), middle (10 to 30 cheetah days) and low (<10 cheetah days). Exposure data were based on the 2012 International Cheetah Studbook, and disease data were based on records on cheetahs dying between 1990 and 2010 retrieved from the species survival plan's official pathologist.

Model Development

- Metapopulation models were designed for a homogenously mixing and a heterogeneously mixing population and were then compared to infection data.
- Each model included three main disease states – susceptible (S), sub-clinically infected (I₁) and clinically infected (I₂) – as well as an environmental component (E).
- Figure 1 represents the model for all six zoos as a homogeneously mixing population.
- Figure 2 represents all six zoos as sub-populations within a metapopulation, producing an overall heterogeneously mixing population.

Fig 1.

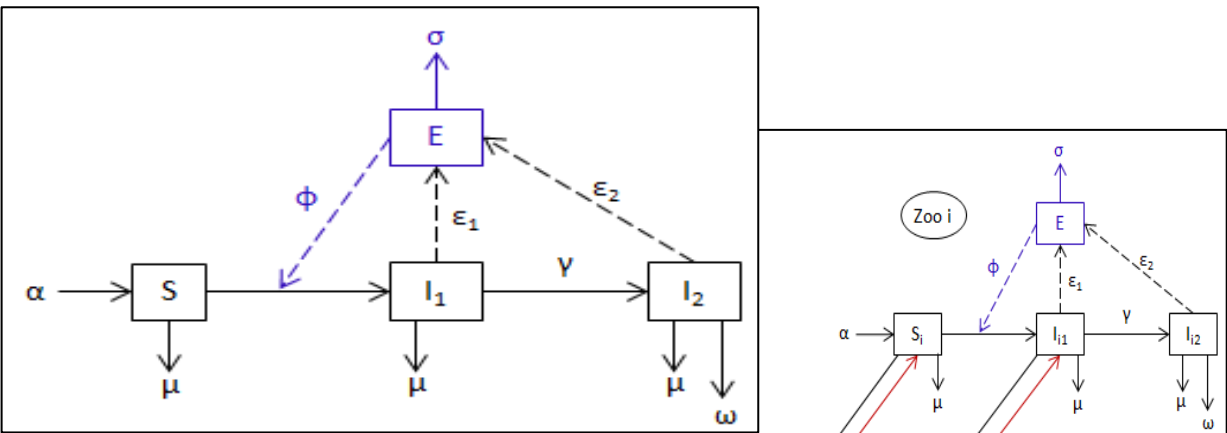


Fig 1. Homogeneously Mixing Population
Fig 2. Heterogeneously Mixing Population

The blue portion represents the environmental component (indirect transmission). In the heterogeneous model, the red and black color-coding is used to represent transfers between any two zoos. It should be noted, however, that any of the six zoos included in the study population interact with all five other zoos.

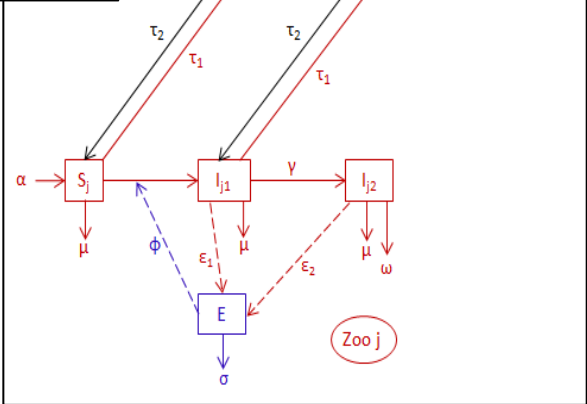


Fig 2.

Model Parameterization and Fitting

- The same demographic and disease data used in the odds ratio calculations were used for model parameterization (demographic) and fitting (disease).
- An expert estimated that the average age at which infected individuals move from subclinical to clinical (1/y) would be at two years of age.
- Estimates of environmental components (ϕ , σ , ϵ_1 , & ϵ_2) were taken from a CWD transmission study in mule deer.⁸
- The model predictions from simulations in R statistical software were compared with disease data visually.

RESULTS

Odds Ratios Calculations

	Odds Ratio	Confidence Interval	P-value
high	(Reference Category)		NA
mid	0.603	0.199-1.787	0.362
low	0.695	0.203-2.320	0.555

Odds ratio for mid-level exposure was 0.603 (p=0.362, CI: 0.199-1.787) and for low-level exposure was 0.695 (p=0.555, CI: 0.203-2.320), so there was no significant effect of exposure to infected cheetahs on development of amyloidosis.

Model Simulations

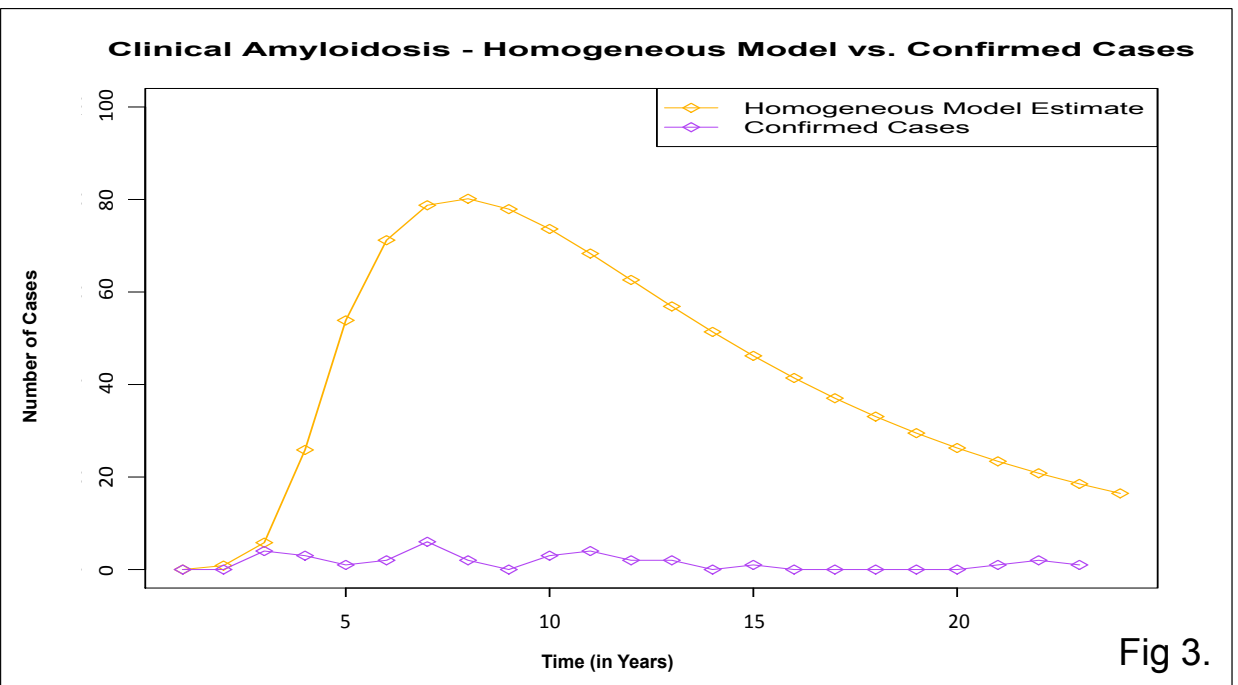


Fig 3.

Figure 3 represents the simulation of a homogenous population. This model estimates a significantly higher number of clinical amyloidosis cases than those seen in necropsy reports.

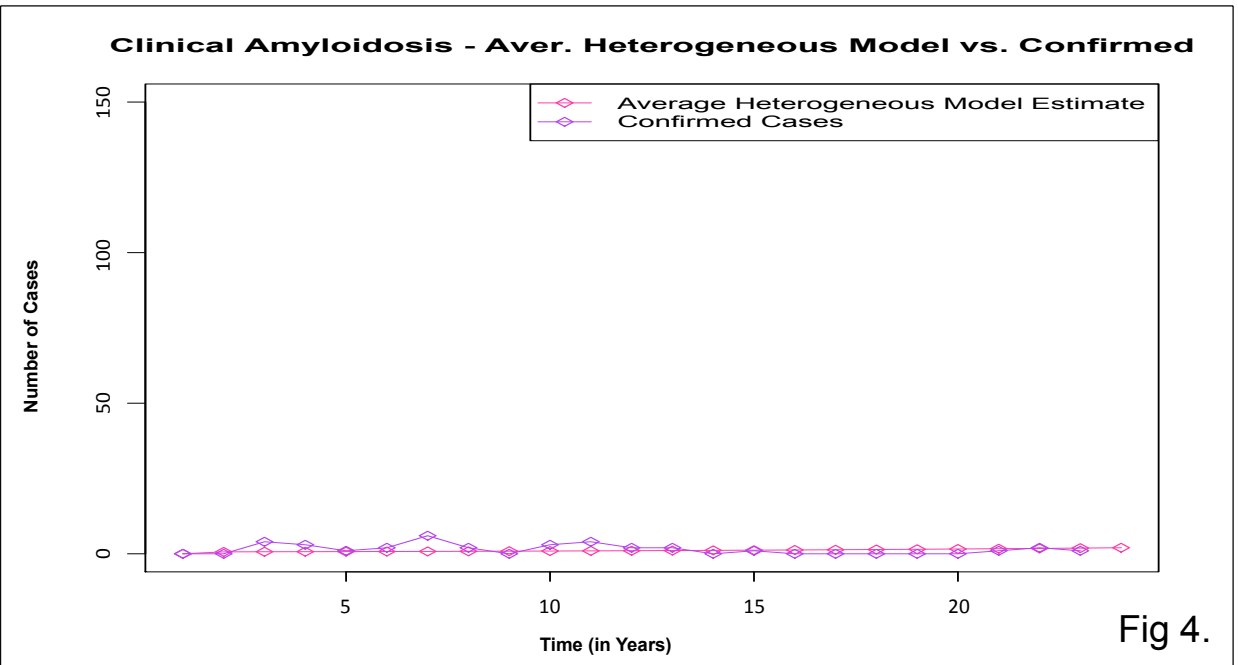


Fig 4.

Figure 4 represents the model simulation of a heterogeneous population. The average estimate produced by the heterogeneous model more accurately reflects the existing data seen in the necropsy reports when compared to the homogeneous model.

CONCLUSIONS

- Simple transmission is not supported based on initial odds ratio calculations.
- The heterogeneous model fits observed data better than the homogeneous model. More details, however, need to go into the model because the heterogeneous model shows an increasing number of amyloidosis cases that are not seen in reality.
- This study used a subset of the captive population. A broader population survey should be pursued.
- Future work will focus on collecting disease data from additional institutions in order to design more complex models and to test more complex hypotheses.
- More complex hypotheses include a genetic component or the need for another inflammatory process to activate the disease.



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